X_1 is from one to six amino acids in length, and

X_2 is from zero to six amino acids in length.

16. (twice amended) A method of inhibiting angiogenesis comprising administering to a mammal an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula X_1-His-Lys-X-Lys-X_2 wherein

X is any amino acid,

X_1 is from zero to twelve amino acids, and

X_2 is from zero to twelve amino acids,

and wherein said compound optionally comprises an amino-terminal protecting group and optionally comprises a carboxy-terminal protecting group.

Remarks

Claims 1-4, 8-9, 16, 19, 22, and 30-49 are pending in the application. Reconsideration is requested in view of the above changes and the following remarks.

Claims 19 and 22 are allowed. Claims 30-35 have been withdrawn from consideration.

A minor error has been corrected in claim 2, and the language has been clarified to more particularly point out and define the relationship of claim 2 with the subject matter of its base claim, claim 1. The inadvertent omission of the word "group" from the last amendment of claim 16 has been rectified.

Regrouping of Claims 30-35

Reconsideration of the restriction requirement is again requested to the extent claims 30-35 are grouped in Group II. The restriction requirement has alleged that these claims are among the claims "drawn to a method of inhibiting endothelial cell proliferation". This is incorrect. Claims 30-35 are directed to compounds per se and are properly grouped in elected

Group I. Claims 30-35 are directed to compounds contained in the pharmaceutical compositions of Group I.

This error in the restriction requirement was pointed out to examiner in the previous response. Examiner did not respond to the argument in the final office action. Reconsideration of the restriction requirement as it relates to claims 30-35, and rejoinder of these claims with elected Group I, is again earnestly solicited.

Response to rejections under 35 U.S.C. § 112 (2)

Claim 16 and 36-49 have been rejected as under 35 U.S.C. 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. The rejection alleges that claim 16 is indefinite because "it is unclear as to the effect of 1-12 additional amino acids in the positions of X_1 and X_2 on the activity of the compound versus having zero amino acids in those positions". The examiner also avers that "it is unclear what effect any amino acid at position X will have on the activity of the claimed compound."

The examiner's action with respect to claim 16 has not set forth a *prima facie* rejection under 35 U.S.C. §112, second paragraph. The primary purpose of §112, second paragraph, is to "ensure that the scope of the claims is clear so that the public is informed of the boundaries of what constitutes infringement of the patent". MPEP §2173. Essentially, a §112, second paragraph rejection seeks to identify and correct ambiguity of claim language or grammatical structure so that the recited scope of the invention is clear to one skilled in the art. Such a rejection is never properly directed to the substance of the claimed invention, but only to the linguistic form of the claim. The sole inquiry under §112, second paragraph, is whether the public would be informed of the boundaries of what constitutes infringement should the claim in question be granted.

It is well-established that "[b]readth of a claim is not to be equated with indefiniteness." *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971); MPEP §2173.04. "If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph." §2173.04.

Examiner has not explained why one skilled in the art would not understand the boundaries of the invention as defined by claim 16. Examiner has not explained why one skilled in the art would fail to understand the meaning of any term set forth in claim 16, or the scope of any individual element in claim 16. Indeed, the principal elements of claim 16 have been defined in the specification. See pages 7-10 for definitions of "amino acid", "N-terminal truncation fragment", and "C-terminal truncation fragment". The same section defines and explains in detail the meaning of the terminology "protected" or "protecting" as used in connection with a group attached to the amino or carboxy terminus of a peptide. Indeed, every term contained in claim 16 which is subject to definition is *defined in the specification.*

The effect of permissible amino acid substitution within X_1, X_2 and X_3 on the activity of the peptide has nothing whatsoever to do with claim definiteness under §112. Examiner's rejection is directed to the substance of the invention, not claim definiteness, and is therefore improper under §112.

The indefiniteness rejection has also been extended to the claims dependent on claim 16, that is, claims 36-49. Examiner has not pointed to any term or feature of any of the dependent claims which would cause one skilled in the art to fail to understand the metes and bounds of the invention claimed in the dependent claims. Indeed, the rejection has been extended to claims such as 42 and 43 which are directed to methods using specific species of peptides whose scope cannot be in doubt (SEQ ID NO:5 and NO:7, respectively).

Reconsideration and withdrawal of the 35 U.S.C. 112, second paragraph, rejection of claims 16 and 36-49 is earnestly solicited,

Response to Rejections under 35 U.S.C. §102

Response to Rejection over Halazonetis et al.

Claims 1-3, 5, 7-10, 12-15 remain rejected as allegedly anticipated by WO 96/25434 and/or U.S. Pat. No. 6,245,886 (collectively "Halazonetis et al."). It is respectfully submitted that Examiner has misconstrued the scope of X_1 in claim 1.

Claim 1 defines a peptide of the formula X_1-His-Lys-X-Lys-X_2 wherein X_1 is the segment His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly (SEQ ID NO:1), or an N-

terminal truncation fragment thereof *containing at least one amino acid.*" The expression "N-terminal truncation fragment" is defined at page 9, lines 29-28 as "a fragment obtained from a parent sequence by removing one or more amino acids *from the N-terminus thereof*". Truncating SEQ ID NO:1 from the N-terminus to the maximum extent possible - i.e., leaving only one original amino acid of SEQ ID NO:1 – results in the single amino acid Glycine (Gly) as X_1. X_1 as defined in amended claim 1 must always contain at a minimum the amino acid Glycine. Thus, the claimed peptide is characterized by the *minimal* sequence **Gly**-His-Lys-X-Lys. X_1 can never be zero amino acids, since this ignores the minimum placed on the length of the N-truncation fragment - "*containing at least one amino acid*".

Halazonetis et al., in pertinent part, discloses the amino acid sequence His-Lys-Ser-Lys-Lys (SEQ ID NO. 21). It can be readily appreciated that the Halazonetis et al. SEQ ID NO: 21 does not set forth each and every element of the minimum sequence of amended claim 1 since it lacks the Glycine residue of the claimed minimal sequence **Gly**-His-Lys-X-Lys.

The Examiner alleges that Halazonetis somehow meets the requirements of claim 1 because "the sequence recited by Halazonetis can be considered to be a truncated fragment having at least one amino acid". This is not what claim 1 states. Examiner is requested to review claim 1 and the definition of "N-terminal truncation fragment" and reconsider the rejection of claim 1. It should be clear that the there is no amino acid sequence in the reference peptide which corresponds to applicant's X_1.

As the Halazonetis et al. references do not recite each and every element of the claimed invention, applicant requests the withdrawal of the rejection relating to these references.

Response to Rejection over Ferreira et al.

Claims 1-4 and 8-9 remain rejected as being allegedly anticipated by Ferreira et al. WO 97/05258, disclosing at page 74 the amino acid sequence Glu-Ala-Pro-His-Lys-Phe-Lys-Asn-Val (as SEQ ID NO:113). Amended claim 1 recites at a minimum the following amino acid sequence: **Gly**-His-Lys-X-Lys. Because X_1 must always contain at least the amino acid

Glycine (Gly), and because Ferreira et al. teach Pro in the position occupied by Gly in the claimed amino acid sequence, Ferreira et al. does not anticipate claim 1.

Dependent claims

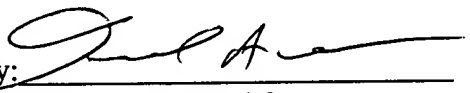
Claims 2-4, 8 and 9 depend from claim 1 and recite additional features of the invention of claim 1. Since claim 1 is not anticipated by the asserted references, neither are these additional claims.

Conclusion

The claims remaining in the application are believed in condition for allowance. An early action toward that end is earnestly solicited.

Respectfully submitted,

KEITH R. McCRAE

By: 

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APPENDIX A: Mark-up of amended claims

2. (amended) The composition of claim 1 wherein

X_1 is from [zero] one to six amino acids in length, and

X_2 is from zero to six amino acids in length.

16. (twice amended) A method of inhibiting angiogenesis comprising administering to a mammal an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula X_1-His-Lys-X-Lys-X_2 wherein

X is any amino acid,

X_1 is from zero to twelve amino acids, and

X_2 is from zero to twelve amino acids,

and wherein said compound optionally comprises an amino-terminal protecting group and optionally comprises a carboxy-terminal protecting group.